210: Investigating the Effect of pH on Cervicovaginal Mucus Barrier Properties to HIV

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1. Understand how changes in pH due to vaginal microbiota can affect mucus barrier properties to HIV
2. Establish whether the temporary elevation in pH from semen exposure also impacts CVM barrier properties, and whether barrier properties to HIV are restored with re-acidification by healthy microbiota (Lactobacilli)

Background

Different vaginal microbiota lead to different properties:
- **Lactobacillus-dominated**
- **Polymicrobial/Bacterial Vaginosis (BV)**

- Lactic acid (LA) producing bacteria (Lactobacilli)
- Few LA producing bacteria
- Low vaginal pH (3-4)
- Increased risk of HIV acquisition
- Trapped in Lactobacillus-dominated sample
- Mobile in Polymicrobial/BV sample

HIV virion mobility differs in cervicovaginal mucus (CVM) from women with different vaginal microbiota:

- % Mobile HIV

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Methods

1. CVM collection with self-sampling method
2. Amsel’s Criteria and Nugent Score (BV diagnosis)
3. Titration of Lactobacillus-dominated samples to determine effect of pH
   - Forward titration: pH incrementally increased with sodium hydroxide (NaOH)
   - Reverse titration: pH increased to 6-7 with NaOH, then incrementally decreased by adding 1 M hydrochloric acid (HCl) or by LA production by Lactobacilli during incubation
4. Addition of fluorescently labeled mCherry-GAG HIV virions
5. Quantitative microscopy technique and particle tracking in recorded movie to determine HIV mobility

Conclusion

- Increasing the pH of CVM from women with Lactobacillus-dominated microbiota leads to a reduction in adhesive interactions with HIV
- HIV virions are mostly freely mobile in CVM from women with BV, regardless of pH adjustment, reflecting lack of adhesive interactions
- Re-acidification of neutralized CVM from women with Lactobacillus-dominated microbiota significantly increases adhesive interactions with HIV virions, an effect observed using both HCl and LA as the acidifying agent
- pH alone is not enough to explain the difference in barrier properties of CVM from women with healthy microbiota (HIV virions adhesively trapped) and CVM from women with BV (HIV virions freely mobile)

Future Directions

- Investigate other factors that could account for differences in HIV trapping (barrier properties) in CVM from women with and without BV, including enzymes produced by microbiota and changes in mucin structure
- Apply results to fortify CVM barrier properties in women with BV to protect against HIV infection